

**Evaluation of CPT-11 in combination with doxorubicin against pancreatic ductal adenocarcinoma PO3 on B6D2F<sub>1</sub> female mice BCM-887 (10.30.96-02.27.97)**

Agent (batch)	Route	Dosage in mg/kg/dose	Schedule in days	Total dose in mg/kg	Fraction of HDT	Drug death (days of death)	Average body weight change in % per mouse at nadir (day of nadir)	Median tumor weight in mg on day 16 (range)	T/C In % day 16	Time for median tumor to reach 1000 mg in days	T-C in days	log cell kill total	Tumor free survivors day 120	Comments
CPT-11	p.o. 0.2 ml	100.8 62.5 38.8	6-9 (2x/day)	806.4 500.0 310.4	1	0/5 0/5 0/5	-16.0 (13) -3.9 (13) -3.5 (13)	75 (0-126) 126 (32-340) 202 (0-1162)	8 14 22	26.2 25.7 20.4	9.8 9.3 4.0	1.3 1.2 0.5	0/5 0/5 0/5	HDT active Active Inactive
Doxorubicin	i.v. 0.2 ml	10.0 6.2 3.8	6-9	20.0 12.4 7.6	1	0/5 0/5 0/5	-14.1 (15) -4.4 (13) -5.1 (15)	0 (0-0) 126 (0-214) 382 (32-546)	0 14 42	25.9 23.9	9.5 7.5	1.2 1.0	4/5 0/5 0/5	HDT highly active Active Active
Doxorubicin CPT-11	i.v/0.2ml po/0.2ml	5.0 80.6 4.1 65.5 3.1 50.4 2.2 35.3 1.2 20.1	6-9 (2x/day)	10.0 644.8 8.2 524.0 6.2 403.2 4.4 282.4 2.4 160.8	0.5) 0.8) 0.41) 0.65) 0.31) 0.50) 0.22) 0.35) 0.12) 0.20)	0/5 0/5 0/5 0/5 0/5 0/5 0/5 0/5 0/5	-10.3 (13) -6.9 (13) -2.5 (8) -3.9 (13) -1.8 (14)	0 (0-0) 0 (0-0) 0 (0-0) 72 (0-126) 336 (270-942)	0 0 0 8 37	52.0 39.9 28.7 20.5	35.6 23.5 12.3 4.1	4.7 3.1 1.6 0.5	1/5 0/5 0/5 0/5	HDT highly active Highly active Highly active Active Inactive
Control								918 (343-1444)		16.4			0/10	

Tumor doubling time = 2.3 days. Mice average weight: CPT-11 = 24.39 g, doxorubicin = 25.26 g, combination = 23.50 g. The 2 administrations of CPT-11 were performed 4 hours apart.

Abbreviation used: HDT = highest dose tested.

Figure 1